
SLIT/ROBO2 Signaling Promotes Mammary Stem Cell Senescence by Inhibiting Wnt Signaling.

Journal: Stem Cell Reports

Publication Year: 2014

Authors: Gwyndolen Harburg, Jennifer Compton, Wei Liu, Naomi Iwai, Shahrzad Zada, Rebecca Marlow, Phyllis Strickland, Yi Ariel Zeng, Lindsay Hinck

PubMed link: 25241737

Funding Grants: UCSC Shared Stem Cell Facility, UCSC CIRM Training Program in Systems Biology of Stem cells

Public Summary:

WNT signaling stimulates the self-renewal of many types of adult stem cells, including mammary stem cells (MaSCs), but mechanisms that limit this activity are poorly understood. Here, we demonstrate that SLIT2 restricts stem cell renewal by signaling through ROBO2 in a subset of basal cells to negatively regulate WNT signaling. The absence of SLIT/ROBO2 signaling leads to increased levels of nuclear beta-catenin. Robo2 loss does not increase the number of stem cells; instead, stem cell renewal is enhanced in the absence of SLIT/ROBO2 signaling. This is due to repressed expression of p16(INK4a), which, in turn, delays MaSC senescence. Together, our studies support a model in which SLITs restrict the expansion of MaSCs by countering the activity of WNTs and limiting self-renewal.

Scientific Abstract:

WNT signaling stimulates the self-renewal of many types of adult stem cells, including mammary stem cells (MaSCs), but mechanisms that limit this activity are poorly understood. Here, we demonstrate that SLIT2 restricts stem cell renewal by signaling through ROBO2 in a subset of basal cells to negatively regulate WNT signaling. The absence of SLIT/ROBO2 signaling leads to increased levels of nuclear beta-catenin. Robo2 loss does not increase the number of stem cells; instead, stem cell renewal is enhanced in the absence of SLIT/ROBO2 signaling. This is due to repressed expression of p16(INK4a), which, in turn, delays MaSC senescence. Together, our studies support a model in which SLITs restrict the expansion of MaSCs by countering the activity of WNTs and limiting self-renewal.

Source URL: <https://www.cirm.ca.gov/about-cirm/publications/slitrobo2-signaling-promotes-mammary-stem-cell-senescence-inhibiting-wnt>